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AMENDMENTS TO THE CLAIMS

Listing of Claims:

This Listing of Claims will replace all prior versions, and listings, of claims in the application:

1-25. (Canceled)

26. (Currently amended) An apparatus for detecting a single nucleotide by Raman spectroscopy

comprising:

a) a reaction chamber;

b) a first channel in fluid communication with the reaction chamber;

c) a second channel in fluid communication with the first channel;

d) a hot spot having a three-dimensional porous structure, the hot spot being stationary within the

second channel and comprising a plurality of cross-linked nanoparticle aggregates affixed within the

hot spot within the second channel, wherein the hot spot enhances nanoparticle aggregates enhance

a Raman signal of the single nucleotide; and

e) a Raman detector operably coupled to the second channel to detect the single nucleotide,

wherein the plurality of cross-linked nanoparticles aggregates affixed within the hot spot within

second channel are packed and stationary crosslinked to form the three-dimensional porous

structure of the hot spot within the second channel; and

f) electrodes adapted to create a field to guide nucleotides from the first channel into the second

channel.

27. (Canceled)

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28. (Canceled)

29. (Previously Presented) The apparatus of claim 26, wherein the first channel is a microfluidic

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channel.

30. (Previously Presented) The apparatus of claim 26, wherein the second channel is a

nanochannel or a microchannel.

31. (Currently amended) The apparatus of claim 26, wherein the portion-plurality of cross-linked

nanoparticle aggregates comprise between two to six nanoparticles per aggregate.

32. (Currently amended) The apparatus of claim 26, wherein the portion-plurality of cross-linked

nanoparticle aggregates comprise two nanoparticles per aggregate.

33. (Currently amended) The apparatus of claim 31, wherein nanoparticles comprising the plurality

of cross-linked nanoparticle aggregates comprise gold and/or silver nanoparticles, and the

nanoparticles are between about 1 nm and 2 µm in size.

34. (Previously Presented) The apparatus of claim 26, wherein the plurality of cross-linked

nanoparticle aggregates affixed within the second channel are throughout a cross sectional area of

the second channel and the Raman detector is adapted to detect said Raman signal.

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35. (New) The apparatus of claim 26, wherein the reaction chamber comprises an exonuclease.

36. (New) The apparatus of claim 26, wherein the single nucleotide is a single unlabeled

nucleotide.

37. (New) The apparatus of claim 26, wherein the single nucleotide is a single Raman labeled

nucleotide.

38. (New) The apparatus of claim 26, further comprising electrodes positioned to create a field to

guide the single nucleotide from the first channel into the second channel such that nucleotides pass

though the hot spot.